DEPARTMENT OF HEALTH & HUMAN SERVICES
New York District

Food & Drug Administration
158-15 Liberty Avenue
Jamaica, New York 11433

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October 16, 2000

WARNING LETTER NYK 2001-02

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dennis Borello, President
Ultratab Laboratories, Inc.
50 Toc Drive
Highland, New York 12528

Dear Mr. Borello:

An inspection of your drug manufacturing facilities located in Highland, New York, conducted by a Food and Drug Administration investigator between July 26-August 24, 2000, found significant deviations from current Good Manufacturing Practice (cGMP) regulations for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, Part 211). Such deviations cause finished pharmaceuticals to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

Our investigation found the following deviations:

1) Failure to reject finished drug products which did not meet established test specifications. Specifically, re-worked Hydrocortisone Cream 1% batch 00E020 had an out of specification (OOS) finished product test result and was released for distribution [211.165].

2) Failure to establish scientifically sound and appropriate specifications, standards and test procedures to assure drug products conform to appropriate standards of identity, strength, quality, and purity. [211.160(b)]. Specifically, the following released products were subjected to repeated testing after failing initial assay results, even though there was no evidence the failing assay results were attributable to laboratory errors:

   (a) DMD Ephedrine/guaifenesin 12.5/200 tablets, batches 00B045, 00B048, and 00B049;
   (b) Bacitracin Ointment batch 00D030.

3) Failure to conduct investigations for the following drug products which did not meet specifications [211.192]:

   (a) Hydrocortisone Cream 1%, batch 00E020, which continued to have an OOS assay value after being reworked;
   (b) Bacitracin Ointment, batch 00D030, which failed initial potency testing;
   (c) DMD Ephedrine/guaifenesin 12.5/200 tablets, batches 00B044, 00B045, 00B046, 00B048, and 00B049, which had out of specification results for tablet hardness.

4) Failure to document the following [211.188]:

   (a) Investigations conducted on DMD Ephedrine/guaifenesin 12.5/200 tablets, batches 00B045, 00B046, 00B047, 00B048, and 00B049 for failed content uniformity;
   (b) Investigations conducted on DMD Ephedrine/guaifenesin 25/200 tablets, batches 99G014 and 99H007 for failed content uniformity;
   (c) The remilling of DMD Ephedrine/guaifenesin 25/200 tablets, batches 99G014 and 99H007.

5) Failure to assure batch uniformity and integrity of products as follows [211.110]:
   (a) In process samples were not analyzed for homogeneity during the reworking of DMD Ephedrine/guaifenesin 25/200 tablets, batches 99G014 and 99H007;
   (b) Process parameters such as tablet weight, thickness and hardness ranges for DMD Ephedrine/guaifenesin were not validated.

6) Failure to conduct an annual review of data to evaluate the quality standards of each drug product to determine the need for changes [211.180(e)].

The above is not intended to be an all-inclusive list of violations. As a manufacturer of finished pharmaceuticals, you are responsible for assuring that your overall operation and the products you manufacture and distribute are in compliance with the law.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these violations and to establish procedures to prevent their recurrence. Failure to promptly correct these violations may result in regulatory action without further notice, such as seizure and/or injunction.

We are in receipt of your firm's August 30, 2000 written response to the observations noted on the Inspectional Observations Form FDA-483. We have the following comments:

The response to FDA-483 point 1 is not satisfactory because it does not address your intentions as to the disposition of Hydrocortisone Cream 1% batch 00E020 currently under your control and in the marketplace. This product did not meet finished product assay specifications and was released without investigation and appropriate testing.

The responses to FDA-483 points 2 and 3 are not satisfactory because they also do not address your intentions as to the disposition of Bacitracin Ointment 1% batch 00D030 and DMD Ephedrine/guaifenesin batches 00B045, 00B048, and 00B049 currently under your control and in the marketplace.

The response to FDA-483 point 4 is not satisfactory because Section 7.1.1c of SOP #QC-08.1 appears to allow retesting by another chemist and subsequent release of the product, even if the investigation shows the initial failing analysis was done correctly. The retesting of samples to invalidate legitimate out of specification results is not an acceptable practice. Drug products failing to meet established standards or specifications and any other relevant quality control criteria must be rejected.

The response to FDA-483 point 5 is not satisfactory because future investigations into batch failures will be initiated, in large part, on products failing USP content uniformity or assay requirements and not for any unexplained discrepancies, such as yield discrepancies. Further, the investigation procedures appear mainly concerned with the adequacy of the raw materials and do not address possible process related causes in sufficient detail.

The response to FDA-483 point 6 indicates that the tablet hardness specifications for DMD Ephedrine/guaifenesine 12.5/200 have been widened. It is not clear as to what criteria you are basing this decision on since the original specification parameters were not validated.

The response to FDA-483 point 8 indicates disagreement with this observation because you maintain your firm had conducted more than a single duplicate assay before releasing the two reworked batches of DMD. Those assays constituted finished product testing. These reworked batches were each split into two separate batches, which were remilled and mixed with additional raw materials to produce four batches. The remilling operation was not documented. In-process samples to assure homogeneity should have been collected and analyzed.

The corrective actions to FDA-483 points 7, and 9 through 19 will be confirmed at a future inspection.

You should reply in writing within 15 working days of the steps you are taking to correct these violations. Correspondence concerning this matter should be directed to the Food and Drug Administration, 300 Hamilton Ave., White Plains, New York 10601, Attention Richard T. Trainor, Compliance Officer.

Sincerely yours,

Robert L. Hart
Acting District Director